



SEQUENCE LISTING

<110> Isis Pharmaceuticals, Inc.

<120> Antisense Modulation Of SMRT Expression

<130> ISPT1004

<150> 10/174,014

<151> 2002-06-17

<160> 75

<170> PatentIn version 3.2

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174

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222

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Tyr	Asp	Glu	Asn	Arg	Lys	Lys	Ala	Glu	Ala	Ala	His	Arg	Ile	Leu	Glu	
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Thr	Arg	Gln	Tyr	His	Glu	Asn	Ile	Lys	Ile	Asn	Gln	Ala	Met	Arg	Lys	
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Lys	Leu	Ile	Leu	Tyr	Phe	Lys	Arg	Arg	Asn	His	Ala	Arg	Lys	Gln	Trp	
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gcc tac ctc ccc acc gcg ccc Ala Tyr Leu Pro Thr Ala Pro 1750 1755	cag ccc ttc agc agc Gln Pro Phe Ser Ser 1760	cgc cac agc Arg His Ser	5445
agc tcc cca ctc tcc cca gga Ser Ser Pro Leu Ser Pro Gly 1765 1770	ggt cca aca cac ttg Gly Pro Thr His Leu 1775	aca aaa cca Thr Lys Pro	5490
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tcc cct cgg acc cag gat gcc Ser Pro Arg Thr Gln Asp Ala 1855 1860	ctc cag cag aga ccc Leu Gln Gln Arg Pro 1865	agt gtg ctt Ser Val Leu	5760
cac aac aca ggc atg aag ggt His Asn Thr Gly Met Lys Gly 1870 1875	atc atc acc gct gtg Ile Ile Thr Ala Val 1880	gag ccc agc Glu Pro Ser	5805
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1930	1935	1940	
gac acc ggc cat gcc ttc ctc Asp Thr Gly His Ala Phe Leu 1945	gcc aag ccc cca gcc cgc tcc ggg Ala Lys Pro Pro Ala Arg Ser Gly 1950	1955	6030
ctg gag ccc gcc tcc tcc ccc Leu Glu Pro Ala Ser Ser Pro 1960	agc aag ggc tcg gag ccc cgg ccc Ser Lys Gly Ser Glu Pro Arg Pro 1965	1970	6075
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ctg gaa gag ctc gac aag agc Leu Glu Glu Leu Asp Lys Ser 2065	cac ctg gag ggg gag gtc cgg ccc His Leu Glu Gly Glu Leu Arg Pro 2070	2075	6390
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agt	gct	gtg	tac	ccg	ctg	ctg	tac	cgg	gat	ggg	gaa	cag	acg	gag	6885
Ser	Ala	Val	Tyr	Pro	Leu	Leu	Tyr	Arg	Asp	Gly	Glu	Gln	Thr	Glu	
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Pro	Ser	Arg	Met	Gly	Ser	Lys	Ser	Pro	Gly	Asn	Thr	Ser	Gln	Pro	
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Pro	Ala	Phe	Phe	Ser	Lys	Leu	Thr	Glu	Ser	Asn	Ser	Ala	Met	Val	
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Lys	Ser	Lys	Lys	Gln	Glu	Ile	Asn	Lys	Lys	Leu	Asn	Thr	His	Asn	
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Arg	Asn	Glu	Pro	Glu	Tyr	Asn	Ile	Ser	Gln	Pro	Gly	Thr	Glu	Ile	
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Phe	Asn	Met	Pro	Ala	Ile	Thr	Gly	Thr	Gly	Leu	Met	Thr	Tyr	Arg	
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Glu	Ser	Pro	Pro	Leu	Ser	Ala	Asn	Ala	Phe	Asn	Pro	Leu	Asn	Ala	
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Ser	Ala	Ser	Leu	Pro	Ala	Ala	Met	Pro	Ile	Thr	Ala	Ala	Asp	Gly	
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Arg	Ser	Asp	His	Thr	Leu	Thr	Ser	Pro	Gly	Gly	Gly	Gly	Lys	Ala	
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Lys	Val	Ser	Gly	Arg	Pro	Ser	Ser	Arg	Lys	Ala	Lys	Ser	Pro	Ala	
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Pro	Gly	Leu	Ala	Ser	Gly	Asp	Arg	Pro	Pro	Ser	Val	Ser	Ser	Val	
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His	Ser	Glu	Gly	Asp	Cys	Asn	Arg	Arg	Thr	Pro	Leu	Thr	Asn	Arg	
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Tyr	Asn	Pro	Leu	Ile	Met	Arg	Leu	Gln	Ala	Gly	Val	Met	Ala	Ser	
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 Pro His His Ala Trp Asp Glu Glu Pro Lys Pro Leu Leu Cys Ser
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<400> 5

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Pro Arg Tyr Pro Pro His Ser Leu Ser Tyr Pro Val Gln Ile Ala Arg
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Thr His Thr Asp Val Gly Leu Leu Glu Tyr Gln His His Ser Arg Asp
35 40 45

Tyr Ala Ser His Leu Ser Pro Gly Ser Ile Ile Gln Pro Gln Arg Arg
50 55 60

Arg Pro Ser Leu Leu Ser Glu Phe Gln Pro Gly Asn Glu Arg Ser Gln

65	70	75	80
Glu Leu His	Leu Arg Pro	Glu Ser His Ser Tyr Leu Pro	Glu Leu Gly
	85	90	95
Lys Ser Glu	Met Glu Phe Ile	Glu Ser Lys Arg Pro Arg	Leu Glu Leu
	100	105	110
Leu Pro Asp	Pro Leu Leu Arg	Pro Ser Pro Leu Leu Ala Thr	Gly Gln
	115	120	125
Pro Ala Gly	Ser Glu Asp	Leu Thr Lys Asp Arg Ser Leu Thr	Gly Lys
	130	135	140
Leu Glu Pro	Val Ser Pro	Pro Ser Pro Pro His Thr Asp	Pro Glu Leu
	145	150	155
Glu Leu Val	Pro Pro Arg	Leu Ser Lys Glu Glu Leu Ile	Gln Asn Met
	165	170	175
Asp Arg Val	Asp Arg Glu Ile	Thr Met Val Glu Gln Gln	Ile Ser Lys
	180	185	190
Leu Lys Lys	Lys Gln Gln Gln	Leu Glu Glu Glu Ala Ala	Lys Pro Pro
	195	200	205
Glu Pro Glu	Lys Pro Val	Ser Pro Pro Pro Ile Glu Ser	Lys His Arg
	210	215	220
Ser Leu Val	Gln Ile Ile Tyr Asp	Glu Asn Arg Lys Lys Ala	Glu Ala
	225	230	235
Ala His Arg	Ile Leu Glu Gly	Leu Gly Pro Gln Val Glu Leu	Pro Leu
	245	250	255
Tyr Asn Gln	Pro Ser Asp Thr Arg	Gln Tyr His Glu Asn Ile	Lys Ile
	260	265	270
Asn Gln Ala	Met Arg Lys Lys	Leu Ile Leu Tyr Phe Lys Arg Arg	Asn
	275	280	285
His Ala Arg	Lys Gln Trp Glu	Gln Lys Phe Cys Gln Arg Tyr Asp	Gln
	290	295	300
Leu Met Glu	Ala Trp Glu Lys Lys	Val Glu Arg Ile Glu Asn Asn	Pro
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Arg Arg Arg	Ala Lys Glu Ser	Lys Val Arg Glu Tyr Tyr Glu	Lys Gln
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Phe Pro Glu	Ile Arg Lys Gln Arg	Glu Leu Gln Glu Arg Met	Gln Arg
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Val Gly Gln Arg Gly Ser Gly Leu Ser Met Ser Pro Ala Arg Ser Glu
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His Glu Val Ser Glu Ile Ile Asp Gly Leu Ser Glu Gln Glu Asn Leu
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Glu Lys Gln Met Arg Gln Leu Ala Val Ile Pro Pro Met Leu Tyr Asp
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Ala Asp Gln Gln Arg Ile Lys Phe Ile Asn Met Asn Gly Leu Met Ala
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Asp Pro Met Lys Val Tyr Lys Asp Arg Gln Val Met Asn Met Trp Ser
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Glu Gln Glu Lys Glu Thr Phe Arg Glu Lys Phe Met Gln His Pro Lys
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Asn Phe Gly Leu Ile Ala Ser Phe Leu Glu Arg Lys Thr Val Ala Glu
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Cys Val Leu Tyr Tyr Tyr Leu Thr Lys Lys Asn Glu Asn Tyr Lys Ser
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Leu Val Arg Arg Ser Tyr Arg Arg Arg Gly Lys Ser Gln Gln Gln Gln
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Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Pro Met Pro
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Arg Ser Ser Gln Glu Glu Lys Asp Glu Lys Glu Lys Glu Lys Glu Ala
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Glu Lys Glu Glu Glu Lys Pro Glu Val Glu Asn Asp Lys Glu Asp Leu
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Leu Lys Glu Lys Thr Asp Asp Thr Ser Gly Glu Asp Asn Asp Glu Lys
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Glu Ala Val Ala Ser Lys Gly Arg Lys Thr Ala Asn Ser Gln Gly Arg
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Arg Lys Gly Arg Ile Thr Arg Ser Met Ala Asn Glu Ala Asn Ser Glu
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Glu Ala Ile Thr Pro Gln Gln Ser Ala Glu Leu Ala Ser Met Glu Leu
 595 600 605

Asn Glu Ser Ser Arg Trp Thr Glu Glu Glu Met Glu Thr Ala Lys Lys
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Gly Leu Leu Glu His Gly Arg Asn Trp Ser Ala Ile Ala Arg Met Val
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Gly Ser Lys Thr Val Ser Gln Cys Lys Asn Phe Tyr Phe Asn Tyr Lys
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 Lys Arg Gln Asn Leu Asp Glu Ile Leu Gln Gln His Lys Leu Lys Met
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 Glu Lys Glu Arg Asn Ala Arg Arg Lys Lys Lys Lys Ala Pro Ala Ala
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 820 825 830
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 850 855 860
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 885 890 895
 Ser Asp Ser Ser Ala Thr Cys Ser Ala Asp Glu Val Asp Glu Ala Glu
 900 905 910
 Gly Gly Asp Lys Asn Arg Leu Leu Ser Pro Arg Pro Ser Leu Leu Thr
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Arg Glu Asp Ser Leu Pro Lys 1250	Gly His Val Ile Tyr 1255	Glu Gly Lys 1260
Lys Gly His Val Leu Ser Tyr 1265	Glu Gly Gly Met Ser 1270	Val Thr Gln 1275
Cys Ser Lys Glu Asp Gly Arg 1280	Ser Ser Ser Gly Pro 1285	Pro His Glu 1290
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Gly Arg Ala Ile Ser Ser Ala 1310	Ser Ile Glu Gly Leu 1315	Met Gly Arg 1320
Ala Ile Pro Pro Glu Arg His 1325	Ser Pro His His Leu 1330	Lys Glu Gln 1335
His His Ile Arg Gly Ser Ile 1340	Thr Gln Gly Ile Pro 1345	Arg Ser Tyr 1350
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Ser Ile His Glu Ile Pro Arg 1415	Glu Glu Leu Arg His 1420	Thr Pro Glu 1425
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Lys Lys His Asp Val Arg Ser Leu Ile Gly Ser Pro Gly Arg Thr
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 Phe Pro Pro Val His Pro Leu Asp Val Met Ala Asp Ala Arg Ala
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 Leu Glu Arg Ala Cys Tyr Glu Glu Ser Leu Lys Ser Arg Pro Gly
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 1685 1690 1695
 Met Leu Arg Gly Leu Ser Pro Arg Glu Ser Ser Leu Ala Leu Asn
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 Tyr Ala Ala Gly Pro Arg Gly Ile Ile Asp Leu Ser Gln Val Pro
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 1865 1870 1875
 Ala Val Glu Pro Ser Lys Pro Thr Val Leu Arg Ser Thr Ser Thr
 1880 1885 1890
 Ser Ser Pro Val Arg Pro Ala Ala Thr Phe Pro Pro Ala Thr His
 1895 1900 1905
 Cys Pro Leu Gly Gly Thr Leu Asp Gly Val Tyr Pro Thr Leu Met
 1910 1915 1920
 Glu Pro Val Leu Leu Pro Lys Glu Ala Pro Arg Val Ala Arg Pro
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 Glu Arg Pro Arg Ala Asp Thr Gly His Ala Phe Leu Ala Lys Pro
 1940 1945 1950
 Pro Ala Arg Ser Gly Leu Glu Pro Ala Ser Ser Pro Ser Lys Gly
 1955 1960 1965
 Ser Glu Pro Arg Pro Leu Val Pro Pro Val Ser Gly His Ala Thr
 1970 1975 1980
 Ile Ala Arg Thr Pro Ala Lys Asn Leu Ala Pro His His Ala Ser
 1985 1990 1995

Pro Asp Pro Pro Ala Pro Pro Ala Ser Ala Ser Asp Pro His Arg
 2000 2005 2010
 Glu Lys Thr Gln Ser Lys Pro Phe Ser Ile Gln Glu Leu Glu Leu
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tcg ccc tat gag cac ctg ctt cgg ggc gtg agt ggc gtg gac ctg Ser Pro Tyr Glu His Leu Leu Arg Gly Val Ser Gly Val Asp Leu 1610 1615 1620	4870
tat cgc agc cac atc ccc ctg gcc ttc gac ccc acc tcc ata ccc Tyr Arg Ser His Ile Pro Leu Ala Phe Asp Pro Thr Ser Ile Pro 1615 1620 1625	4915

1625	1630	1635	
cgc ggc atc cct ctg gac gca gcc gct gcc tac tac ctg ccc cga Arg Gly Ile Pro Leu Asp Ala Ala Ala Ala Tyr Tyr Leu Pro Arg 1640 1645 1650			4960
cac ctg gcc ccc aac ccc acc tac ccg cac ctg tac cca ccc tac His Leu Ala Pro Asn Pro Thr Tyr Pro His Leu Tyr Pro Pro Tyr 1655 1660 1665			5005
ctc atc cgc ggc tac ccc gac acg gcg gcg ctg gag aac cgg cag Leu Ile Arg Gly Tyr Pro Asp Thr Ala Ala Leu Glu Asn Arg Gln 1670 1675 1680			5050
acc atc atc aat gac tac atc acc tcg cag cag atg cac cac aac Thr Ile Ile Asn Asp Tyr Ile Thr Ser Gln Gln Met His His Asn 1685 1690 1695			5095
acg gcc acc gcc atg gcc cag cga gct gat atg ctg agg ggc ctc Thr Ala Thr Ala Met Ala Gln Arg Ala Asp Met Leu Arg Gly Leu 1700 1705 1710			5140
tcg ccc cgc gag tcc tcg ctg gca ctc aac tac gct gcg ggt ccc Ser Pro Arg Glu Ser Ser Leu Ala Leu Asn Tyr Ala Ala Gly Pro 1715 1720 1725			5185
cga ggc atc atc gac ctg tcc caa gtg cca cac ctg cct gtg ctc Arg Gly Ile Ile Asp Leu Ser Gln Val Pro His Leu Pro Val Leu 1730 1735 1740			5230
gtg ccc ccg aca cca ggc acc cca gcc acc gcc atg gac cgc ctt Val Pro Pro Thr Pro Gly Thr Pro Ala Thr Ala Met Asp Arg Leu 1745 1750 1755			5275
gcc tac ctc ccc acc gcg ccc cag ccc ttc agc agc cgc cac agc Ala Tyr Leu Pro Thr Ala Pro Gln Pro Phe Ser Ser Arg His Ser 1760 1765 1770			5320
agc tcc cca ctc tcc cca gga ggt cca aca cac ttg aca aaa cca Ser Ser Pro Leu Ser Pro Gly Gly Pro Thr His Leu Thr Lys Pro 1775 1780 1785			5365
acc acc acg tcc tcg tcc gag cgg gag cga gac cgg gat cga gag Thr Thr Thr Ser Ser Ser Glu Arg Glu Arg Asp Arg Asp Arg Glu 1790 1795 1800			5410
cgg gac cgg gat cgg gag cgg gaa aag tcc atc ctc acg tcc acc Arg Asp Arg Asp Arg Glu Arg Glu Lys Ser Ile Leu Thr Ser Thr 1805 1810 1815			5455
acg acg gtg gag cac gca ccc atc tgg aga cct ggt aca gag cag Thr Thr Val Glu His Ala Pro Ile Trp Arg Pro Gly Thr Glu Gln 1820 1825 1830			5500
agc agc ggc agc agc ggc agc agc ggc ggg ggt ggg ggc agc agc Ser Ser Gly Ser Ser Gly Ser Ser Gly Gly Gly Gly Gly Ser Ser 1835 1840 1845			5545
agc cgc ccc gcc tcc cac tcc cat gcc cac cag cac tcg ccc atc Ser Arg Pro Ala Ser His Ser His Ala His Gln His Ser Pro Ile 1850 1855 1860			5590
tcc cct cgg acc cag gat gcc ctc cag cag aga ccc agt gtg ctt Ser Pro Arg Thr Gln Asp Ala Leu Gln Gln Arg Pro Ser Val Leu 1865 1870 1875			5635
cac aac aca ggc atg aag ggt atc atc acc gct gtg gag ccc agc His Asn Thr Gly Met Lys Gly Ile Ile Thr Ala Val Glu Pro Ser 1880 1885 1890			5680
aag ccc acg gtc ctg agg tcc acc tcc acc tcc tca ccc gtt cgc			5725

Lys	Pro	Thr	Val	Leu	Arg	Ser	Thr	Ser	Thr	Ser	Ser	Pro	Val	Arg	
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cca	gct	gcc	aca	ttc	cca	cct	gcc	acc	cac	tgc	cca	ctg	ggc	ggc	5770
Pro	Ala	Ala	Thr	Phe	Pro	Pro	Ala	Thr	His	Cys	Pro	Leu	Gly	Gly	
1910						1915					1920				
acc	ctc	gat	ggg	gtc	tac	cct	acc	ctc	atg	gag	ccc	gtc	ttg	ctg	5815
Thr	Leu	Asp	Gly	Val	Tyr	Pro	Thr	Leu	Met	Glu	Pro	Val	Leu	Leu	
1925						1930					1935				
ccc	aag	gag	gcc	ccc	cgg	gtc	gcc	cgg	cca	gag	cgg	ccc	cga	gca	5860
Pro	Lys	Glu	Ala	Pro	Arg	Val	Ala	Arg	Pro	Glu	Arg	Pro	Arg	Ala	
1940						1945					1950				
gac	acc	ggc	cat	gcc	ttc	ctc	gcc	aag	ccc	cca	gcc	cgc	tcc	ggg	5905
Asp	Thr	Gly	His	Ala	Phe	Leu	Ala	Lys	Pro	Pro	Ala	Arg	Ser	Gly	
1955						1960					1965				
ctg	gag	ccc	gcc	tcc	tcc	ccc	agc	aag	ggc	tgc	gag	ccc	cgg	ccc	5950
Leu	Glu	Pro	Ala	Ser	Ser	Pro	Ser	Lys	Gly	Ser	Glu	Pro	Arg	Pro	
1970						1975					1980				
cta	gtg	cct	cct	gtc	tct	ggc	cac	gcc	acc	atc	gcc	cgc	acc	cct	5995
Leu	Val	Pro	Pro	Val	Ser	Gly	His	Ala	Thr	Ile	Ala	Arg	Thr	Pro	
1985						1990					1995				
gcg	aag	aac	ctc	gca	cct	cac	cac	gcc	agc	ccg	gac	ccg	ccg	gcg	6040
Ala	Lys	Asn	Leu	Ala	Pro	His	His	Ala	Ser	Pro	Asp	Pro	Pro	Ala	
2000						2005					2010				
cca	cct	gcc	tgc	gcc	tgc	gac	ccg	cac	cgg	gaa	aag	act	caa	agt	6085
Pro	Pro	Ala	Ser	Ala	Ser	Asp	Pro	His	Arg	Glu	Lys	Thr	Gln	Ser	
2015						2020					2025				
aaa	ccc	ttt	tcc	atc	cag	gaa	ctg	gaa	ctc	cgt	tct	ctg	ggt	tac	6130
Lys	Pro	Phe	Ser	Ile	Gln	Glu	Leu	Glu	Leu	Arg	Ser	Leu	Gly	Tyr	
2030						2035					2040				
cac	ggc	agc	agc	tac	agc	ccc	gaa	ggg	gtg	gag	ccc	gtc	agc	cct	6175
His	Gly	Ser	Ser	Tyr	Ser	Pro	Glu	Gly	Val	Glu	Pro	Val	Ser	Pro	
2045						2050					2055				
gtg	agc	tca	ccc	agt	ctg	acc	cac	gac	aag	ggg	ctc	ccc	aag	cac	6220
Val	Ser	Ser	Pro	Ser	Leu	Thr	His	Asp	Lys	Gly	Leu	Pro	Lys	His	
2060						2065					2070				
ctg	gaa	gag	ctc	gac	aag	agc	cac	ctg	gag	ggg	gag	ctg	cgg	ccc	6265
Leu	Glu	Glu	Leu	Asp	Lys	Ser	His	Leu	Glu	Gly	Glu	Leu	Arg	Pro	
2075						2080					2085				
aag	cag	cca	ggc	ccc	gtg	aag	ctt	ggc	ggg	gag	gcc	gcc	cac	ctc	6310
Lys	Gln	Pro	Gly	Pro	Val	Lys	Leu	Gly	Gly	Glu	Ala	Ala	His	Leu	
2090						2095					2100				
cca	cac	ctg	cgg	ccg	ctg	cct	gag	agc	cag	ccc	tgc	tcc	agc	ccg	6355
Pro	His	Leu	Arg	Pro	Leu	Pro	Glu	Ser	Gln	Pro	Ser	Ser	Ser	Pro	
2105						2110					2115				
ctg	ctc	cag	acc	gcc	cca	ggg	gtc	aaa	ggt	cac	cag	cgg	gtg	gtc	6400
Leu	Leu	Gln	Thr	Ala	Pro	Gly	Val	Lys	Gly	His	Gln	Arg	Val	Val	
2120						2125					2130				
acc	ctg	gcc	cag	cac	atc	agt	gag	gtc	atc	aca	cag	gac	tac	acc	6445
Thr	Leu	Ala	Gln	His	Ile	Ser	Glu	Val	Ile	Thr	Gln	Asp	Tyr	Thr	
2135						2140					2145				
cgg	cac	cac	cca	cag	cag	ctc	agc	gca	ccc	ctg	ccc	gcc	ccc	ctc	6490
Arg	His	His	Pro	Gln	Gln	Leu	Ser	Ala	Pro	Leu	Pro	Ala	Pro	Leu	
2150						2155					2160				

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cca ccc agt gac ctc tac ctc ccg ccc ccg gac cat ggt gcc ccg Pro Pro Ser Asp Leu Tyr Leu Pro Pro Pro Asp His Gly Ala Pro 2180 2185 2190	6580
gcc cgt ggc tcc ccc cac agc gaa ggg ggc aag agg tct cca gag Ala Arg Gly Ser Pro His Ser Glu Gly Gly Lys Arg Ser Pro Glu 2195 2200 2205	6625
cca aac aag acg tcg gtc ttg ggt ggt ggt gag gac ggt att gaa Pro Asn Lys Thr Ser Val Leu Gly Gly Gly Glu Asp Gly Ile Glu 2210 2215 2220	6670
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agt gct gtg tac ccg ctg ctg tac ccg gat ggg gaa cag acg gag Ser Ala Val Tyr Pro Leu Leu Tyr Arg Asp Gly Glu Gln Thr Glu 2240 2245 2250	6760
ccc agc agg atg ggc tcc aag tct cca ggc aac acc agc cag ccg Pro Ser Arg Met Gly Ser Lys Ser Pro Gly Asn Thr Ser Gln Pro 2255 2260 2265	6805
cca gcc ttc ttc agc aag ctg acc gag agc aac tcc gcc atg gtc Pro Ala Phe Phe Ser Lys Leu Thr Glu Ser Asn Ser Ala Met Val 2270 2275 2280	6850
aag tcc aag aag caa gag atc aac aag aag ctg aac acc cac aac Lys Ser Lys Lys Gln Glu Ile Asn Lys Lys Leu Asn Thr His Asn 2285 2290 2295	6895
cgg aat gag cct gaa tac aat atc agc cag cct ggg acg gag atc Arg Asn Glu Pro Glu Tyr Asn Ile Ser Gln Pro Gly Thr Glu Ile 2300 2305 2310	6940
ttc aat atg ccc gcc atc acc gga aca ggc ctt atg acc tat aga Phe Asn Met Pro Ala Ile Thr Gly Thr Gly Leu Met Thr Tyr Arg 2315 2320 2325	6985
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gcc ata att aga aag gca ctc atg ggt aaa tat gac cag tgg gaa Ala Ile Ile Arg Lys Ala Leu Met Gly Lys Tyr Asp Gln Trp Glu 2345 2350 2355	7075
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 His Ser Glu Gly Asp Cys Asn Arg Arg Thr Pro Leu Thr Asn Arg
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 gtg tgg gag gac agg ccc tcg tcc gca ggt tcc acg cca ttc ccc 7390
 Val Trp Glu Asp Arg Pro Ser Ser Ala Gly Ser Thr Pro Phe Pro
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 tac aac ccc ctg atc atg cgg ctg cag gcg ggt gtc atg gct tcc 7435
 Tyr Asn Pro Leu Ile Met Arg Leu Gln Ala Gly Val Met Ala Ser
 2465 2470 2475
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 Pro Pro Pro Pro Gly Leu Pro Ala Gly Ser Gly Pro Leu Ala Gly
 2480 2485 2490
 ccc cac cac gcc tgg gac gag gag ccc aag cca ctg ctc tgc tcg 7525
 Pro His His Ala Trp Asp Glu Glu Pro Lys Pro Leu Leu Cys Ser
 2495 2500 2505
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 Gln Tyr Glu Thr Leu Ser Asp Ser Glu
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 <212> PRT
 <213> Homo sapiens

<400> 13

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 20 25 30
 Thr His Thr Asp Val Gly Leu Leu Glu Tyr Gln His His Ser Arg Asp
 35 40 45
 Tyr Ala Ser His Leu Ser Pro Gly Ser Ile Ile Gln Pro Gln Arg Arg
 50 55 60
 Arg Pro Ser Leu Leu Ser Glu Phe Gln Pro Gly Asn Glu Arg Ser Gln
 65 70 75 80
 Glu Leu His Leu Arg Pro Glu Ser His Ser Tyr Leu Pro Glu Leu Gly
 85 90 95
 Lys Ser Glu Met Glu Phe Ile Glu Ser Lys Arg Pro Arg Leu Glu Leu
 100 105 110
 Leu Pro Asp Pro Leu Leu Arg Pro Ser Pro Leu Leu Ala Thr Gly Gln
 115 120 125
 Pro Ala Gly Ser Glu Asp Leu Thr Lys Asp Arg Ser Leu Thr Gly Lys
 130 135 140
 Leu Glu Pro Val Ser Pro Pro Ser Pro Pro His Thr Asp Pro Glu Leu
 145 150 155 160
 Glu Leu Val Pro Pro Arg Leu Ser Lys Glu Glu Leu Ile Gln Asn Met
 165 170 175
 Asp Arg Val Asp Arg Glu Ile Thr Met Val Glu Gln Gln Ile Ser Lys
 180 185 190
 Leu Lys Lys Lys Gln Gln Gln Leu Glu Glu Glu Ala Ala Lys Pro Pro
 195 200 205
 Glu Pro Glu Lys Pro Val Ser Pro Pro Pro Ile Glu Ser Lys His Arg
 210 215 220
 Ser Leu Val Gln Ile Ile Tyr Asp Glu Asn Arg Lys Lys Ala Glu Ala
 225 230 235 240
 Ala His Arg Ile Leu Glu Gly Leu Gly Pro Gln Val Glu Leu Pro Leu
 245 250 255
 Tyr Asn Gln Pro Ser Asp Thr Arg Gln Tyr His Glu Asn Ile Lys Ile
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 Asn Gln Ala Met Arg Lys Lys Leu Ile Leu Tyr Phe Lys Arg Arg Asn
 275 280 285
 His Ala Arg Lys Gln Trp Lys Gln Lys Phe Cys Gln Arg Tyr Asp Gln
 290 295 300

Leu Met Glu Ala Leu Glu Lys Lys Val Glu Arg Ile Glu Asn Asn Pro
 305 310 315 320
 Arg Arg Arg Ala Lys Glu Ser Lys Val Arg Glu Tyr Tyr Glu Lys Gln
 325 330 335
 Phe Pro Glu Ile Arg Lys Gln Arg Glu Leu Gln Glu Arg Met Gln Ser
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 Arg Val Gly Gln Arg Gly Ser Gly Leu Ser Met Ser Ala Ala Arg Ser
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 Glu His Glu Val Ser Glu Ile Ile Asp Gly Leu Ser Glu Gln Glu Asn
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 Leu Glu Lys Gln Met Arg Gln Leu Ala Val Ile Pro Pro Met Leu Tyr
 385 390 395 400
 Asp Ala Asp Gln Gln Arg Ile Lys Phe Ile Asn Met Asn Gly Leu Met
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 Ala Asp Pro Met Lys Val Tyr Lys Asp Arg Gln Val Met Asn Met Trp
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 Ser Glu Gln Glu Lys Glu Thr Phe Arg Glu Lys Phe Met Gln His Pro
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 Lys Asn Phe Gly Leu Ile Ala Ser Phe Leu Glu Arg Lys Thr Val Ala
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 Glu Cys Val Leu Tyr Tyr Tyr Leu Thr Lys Lys Asn Glu Asn Tyr Lys
 465 470 475 480
 Ser Leu Val Arg Arg Ser Tyr Arg Arg Arg Gly Lys Ser Gln Gln Gln
 485 490 495
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 Pro Arg Ser Ser Gln Glu Glu Lys Asp Glu Lys Glu Lys Glu Lys Glu
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 Ala Glu Lys Glu Glu Glu Lys Pro Glu Val Glu Asn Asp Lys Glu Asp
 530 535 540
 Leu Leu Lys Glu Lys Thr Asp Asp Thr Ser Gly Glu Asp Asn Asp Glu
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 565 570 575
 Arg Arg Lys Gly Arg Ile Thr Arg Ser Met Ala Asn Glu Ala Asn Ser
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Glu Glu Ala Ile Thr Pro Gln Gln Ser Ala Glu Leu Ala Ser Met Glu
 595 600 605
 Leu Asn Glu Ser Ser Arg Trp Thr Glu Glu Glu Met Glu Thr Ala Lys
 610 615 620
 Lys Gly Leu Leu Glu His Gly Arg Asn Trp Ser Ala Ile Ala Arg Met
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 Val Gly Ser Lys Thr Val Ser Gln Cys Lys Asn Phe Tyr Phe Asn Tyr
 645 650 655
 Lys Lys Arg Gln Asn Leu Asp Glu Ile Leu Gln Gln His Lys Leu Lys
 660 665 670
 Met Glu Lys Glu Arg Asn Ala Arg Arg Lys Lys Lys Lys Ala Pro Ala
 675 680 685
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 690 695 700
 Met Glu Ala Ser Gly Val Ser Gly Asn Glu Glu Glu Met Val Glu Glu
 705 710 715 720
 Ala Glu Ala Leu His Ala Ser Gly Asn Glu Val Pro Arg Gly Glu Cys
 725 730 735
 Ser Gly Pro Ala Thr Val Asn Asn Ser Ser Asp Thr Glu Ser Ile Pro
 740 745 750
 Ser Pro His Thr Glu Ala Ala Lys Asp Thr Gly Gln Asn Gly Pro Lys
 755 760 765
 Pro Pro Ala Thr Leu Gly Ala Asp Gly Pro Pro Pro Gly Pro Pro Thr
 770 775 780
 Pro Pro Arg Arg Thr Ser Arg Ala Pro Ile Glu Pro Thr Pro Ala Ser
 785 790 795 800
 Glu Ala Thr Gly Ala Pro Thr Pro Pro Pro Ala Pro Pro Ser Pro Ser
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 Ala Pro Pro Pro Val Val Pro Lys Glu Glu Lys Glu Glu Glu Thr Ala
 820 825 830
 Ala Ala Pro Pro Val Glu Glu Gly Glu Glu Gln Lys Pro Pro Ala Ala
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 Glu Glu Leu Ala Val Asp Thr Gly Lys Ala Glu Glu Pro Val Lys Ser
 850 855 860
 Glu Cys Thr Glu Glu Ala Glu Glu Gly Pro Ala Lys Gly Lys Asp Ala

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Glu Ala Ala Glu Ala Thr Ala Glu Gly Ala Leu Lys Ala Glu Lys Lys	885	890	895
Glu Gly Gly Ser Gly Arg Ala Thr Thr Ala Lys Ser Ser Gly Ala Pro	900	905	910
Gln Asp Ser Asp Ser Ser Ala Thr Cys Ser Ala Asp Glu Val Asp Glu	915	920	925
Ala Glu Gly Gly Asp Lys Asn Arg Leu Leu Ser Pro Arg Pro Ser Leu	930	935	940
Leu Thr Pro Thr Gly Asp Pro Arg Ala Asn Ala Ser Pro Gln Lys Pro	945	950	955
Leu Asp Leu Lys Gln Leu Lys Gln Arg Ala Ala Ala Ile Pro Pro Ile	965	970	975
Gln Val Thr Lys Val His Glu Pro Pro Arg Glu Asp Ala Ala Pro Thr	980	985	990
Lys Pro Ala Pro Pro Ala Pro Pro Pro Pro Gln Asn Leu Gln Pro Glu	995	1000	1005
Ser Asp Ala Pro Gln Gln Pro Gly Ser Ser Pro Arg Gly Lys Ser	1010	1015	1020
Arg Ser Pro Ala Pro Pro Ala Asp Lys Glu Ala Phe Ala Ala Glu	1025	1030	1035
Ala Gln Lys Leu Pro Gly Asp Pro Pro Cys Trp Thr Ser Gly Leu	1040	1045	1050
Pro Phe Pro Val Pro Pro Arg Glu Val Ile Lys Ala Ser Pro His	1055	1060	1065
Ala Pro Asp Pro Ser Ala Phe Ser Tyr Ala Pro Pro Gly His Pro	1070	1075	1080
Leu Pro Leu Gly Leu His Asp Thr Ala Arg Pro Val Leu Pro Arg	1085	1090	1095
Pro Pro Thr Ile Ser Asn Pro Pro Pro Leu Ile Ser Ser Ala Lys	1100	1105	1110
His Pro Ser Val Leu Glu Arg Gln Ile Gly Ala Ile Ser Gln Gly	1115	1120	1125
Met Ser Val Gln Leu His Val Pro Tyr Ser Glu His Ala Lys Ala	1130	1135	1140

Pro Val Gly Pro Val Thr Met Gly Leu Pro Leu Pro Met Asp Pro
1145 1150 1155

Lys Lys Leu Ala Pro Phe Ser Gly Val Lys Gln Glu Gln Leu Ser
1160 1165 1170

Pro Arg Gly Gln Ala Gly Pro Pro Glu Ser Leu Gly Val Pro Thr
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Ala Gln Glu Ala Ser Val Leu Arg Gly Thr Ala Leu Gly Ser Val
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Pro Gly Gly Ser Ile Thr Lys Gly Ile Pro Ser Thr Arg Val Pro
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Ser Asp Ser Ala Ile Thr Tyr Arg Gly Ser Ile Thr His Gly Thr
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Pro Ala Asp Val Leu Tyr Lys Gly Thr Ile Thr Arg Ile Ile Gly
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Glu Asp Ser Pro Ser Arg Leu Asp Arg Gly Arg Glu Asp Ser Leu
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Pro Lys Gly His Val Ile Tyr Glu Gly Lys Lys Gly His Val Leu
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Ser Tyr Glu Gly Gly Met Ser Val Thr Gln Cys Ser Lys Glu Asp
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Gly Arg Ser Ser Ser Gly Pro Pro His Glu Thr Ala Ala Pro Lys
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Arg Thr Tyr Asp Met Met Glu Gly Arg Val Gly Arg Ala Ile Ser
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Ser Ala Ser Ile Glu Gly Leu Met Gly Arg Ala Ile Pro Pro Glu
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Arg His Ser Pro His His Leu Lys Glu Gln His His Ile Arg Gly
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Ser Ile Thr Gln Gly Ile Pro Arg Ser Tyr Val Glu Ala Gln Glu
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Asp Tyr Leu Arg Arg Glu Ala Lys Leu Leu Lys Arg Glu Gly Thr
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Pro Pro Pro Pro Pro Ser Arg Asp Leu Thr Glu Ala Tyr Lys
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Thr Gln Ala Leu Gly Pro Leu Lys Leu Lys Pro Ala His Glu Gly
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Leu Val Ala Thr Val Lys Glu Ala Gly Arg Ser Ile His Glu Ile
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 Arg Pro Leu Lys Glu Gly Ser Ile Thr Gln Gly Thr Pro Leu Lys
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 Tyr Asp Thr Gly Ala Ser Thr Thr Gly Ser Lys Lys His Asp Val
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 Glu Pro Thr Pro Arg Leu Gln Glu Gly Ser Leu Ser Ser Ser Lys
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 Ala Ser Gln Asp Arg Lys Leu Thr Ser Thr Pro Arg Glu Ile Ala
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 Lys Ser Pro His Ser Thr Val Pro Glu His His Pro His Pro Ile
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 Ser Pro Tyr Glu His Leu Leu Arg Gly Val Ser Gly Val Asp Leu
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 Tyr Arg Ser His Ile Pro Leu Ala Phe Asp Pro Thr Ser Ile Pro
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 Arg Gly Ile Pro Leu Asp Ala Ala Ala Ala Tyr Tyr Leu Pro Arg
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 His Leu Ala Pro Asn Pro Thr Tyr Pro His Leu Tyr Pro Pro Tyr
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 Leu Ile Arg Gly Tyr Pro Asp Thr Ala Ala Leu Glu Asn Arg Gln
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Thr Ile Ile Asn Asp Tyr Ile Thr Ser Gln Gln Met His His Asn
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 Thr Ala Thr Ala Met Ala Gln Arg Ala Asp Met Leu Arg Gly Leu
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 Ser Pro Arg Glu Ser Ser Leu Ala Leu Asn Tyr Ala Ala Gly Pro
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 Arg Gly Ile Ile Asp Leu Ser Gln Val Pro His Leu Pro Val Leu
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 Val Pro Pro Thr Pro Gly Thr Pro Ala Thr Ala Met Asp Arg Leu
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 Ala Tyr Leu Pro Thr Ala Pro Gln Pro Phe Ser Ser Arg His Ser
 1760 1765 1770
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 Thr Thr Thr Ser Ser Ser Glu Arg Glu Arg Asp Arg Asp Arg Glu
 1790 1795 1800
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 Thr Thr Val Glu His Ala Pro Ile Trp Arg Pro Gly Thr Glu Gln
 1820 1825 1830
 Ser Ser Gly Ser Ser Gly Ser Ser Gly Gly Gly Gly Gly Ser Ser
 1835 1840 1845
 Ser Arg Pro Ala Ser His Ser His Ala His Gln His Ser Pro Ile
 1850 1855 1860
 Ser Pro Arg Thr Gln Asp Ala Leu Gln Gln Arg Pro Ser Val Leu
 1865 1870 1875
 His Asn Thr Gly Met Lys Gly Ile Ile Thr Ala Val Glu Pro Ser
 1880 1885 1890
 Lys Pro Thr Val Leu Arg Ser Thr Ser Thr Ser Ser Pro Val Arg
 1895 1900 1905
 Pro Ala Ala Thr Phe Pro Pro Ala Thr His Cys Pro Leu Gly Gly
 1910 1915 1920
 Thr Leu Asp Gly Val Tyr Pro Thr Leu Met Glu Pro Val Leu Leu
 1925 1930 1935
 Pro Lys Glu Ala Pro Arg Val Ala Arg Pro Glu Arg Pro Arg Ala

1940	1945	1950
Asp Thr Gly His Ala Phe Leu 1955 1960	Ala Lys Pro Pro	Ala Arg Ser Gly 1965
Leu Glu Pro Ala Ser Ser Pro 1970 1975	Ser Lys Gly Ser	Glu Pro Arg Pro 1980
Leu Val Pro Pro Val Ser Gly 1985 1990	His Ala Thr Ile	Ala Arg Thr Pro 1995
Ala Lys Asn Leu Ala Pro His 2000 2005	His Ala Ser Pro	Asp Pro Pro Ala 2010
Pro Pro Ala Ser Ala Ser Asp 2015 2020	Pro His Arg Glu	Lys Thr Gln Ser 2025
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His Gly Ser Ser Tyr Ser Pro 2045 2050	Glu Gly Val Glu	Pro Val Ser Pro 2055
Val Ser Ser Pro Ser Leu Thr 2060 2065	His Asp Lys Gly	Leu Pro Lys His 2070
Leu Glu Glu Leu Asp Lys Ser 2075 2080	His Leu Glu Gly	Glu Leu Arg Pro 2085
Lys Gln Pro Gly Pro Val Lys 2090 2095	Leu Gly Gly Glu	Ala Ala His Leu 2100
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